AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A conjugate comprising a carrier substituted with one or more occurrences of a moiety having the structure:

wherein each occurrence of M is independently a modifier; and each occurrence of L^M is independently an oxime-containing linker.

2. (Original) The conjugate of claim 1, wherein each occurrence of L^M is independently a moiety having the structure:

wherein each occurrence of L^{M1} is independently a substituted or unsubstituted, cyclic or acyclic, linear or branched C₀₋₁₂alkylidene or C₀₋₁₂alkenylidene moiety wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl.

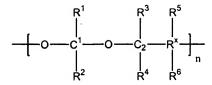
- 3. (Original) The conjugate of claim 2, wherein one or more occurrences of L^{M1} independently comprises a maleimide- or N-hydroxysuccinimide ester-containing crosslinker.
- 4. (Original) The conjugate of claim 3, wherein one or more occurrences of L^{M1} independently comprises a 4-(N-maleimidomethyl)cyclohexane-1-carboxylate, m-maleimidobenzoyl or a 4-(p-maleimidophenyl)butyrate crosslinker.

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- 5. (Original) The conjugate of claim 1, wherein one or more occurrences of M comprises, or is attached to the carrier through, a biodegradable bond.
- 6. (Original) The conjugate of claim 4, wherein the biodegradable bond is selected from the group consisting of acetal, ketal, amide, ester, thioester, enamine, imine, imide, dithio, and phosphoester bond.
- 7. (Original) The conjugate of claim 1, wherein the carrier is a hydrophilic biodegradable polymer selected from the group consisting of carbohydrates, glycopolysaccharides, glycolipids, glycoconjugates, polyacetals, polyketals, and derivatives thereof.
- 8. (Original) The conjugate of claim 1, wherein the carrier is a naturally occurring linear and branched biodegradable biocompatible homopolysaccharide selected from the group consisting of cellulose, amylose, dextran, levan, fucoidan, carraginan, inulin, pectin, amylopectin, glycogen and lixenan.
- 9. (Original) The conjugate of claim 1, wherein the carrier is a naturally occurring linear and branched biodegradable biocompatible heteropolysaccharide selected from the group consisting of agarose, hyluronan, chondroitinsulfate, dermatansulfate, keratansulfate, alginic acid and heparin.
- 10. **(Original)** The conjugate of claim 1, wherein the carrier is a hydrophilic polymer selected from the group consisting of polyacrylates, polyvinyl polymers, polyesters, polyorthoesters, polyamides, polypeptides, and derivatives thereof.
- 11. (Original) The conjugate of claim 1, wherein the carrier is a biodegradable biocompatible polyacetal wherein at least a subset of the polyacetal repeat structural units have the following chemical structure:

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wherein for each occurrence of the n bracketed structure, one of R¹ and R² is hydrogen, and the other is a biocompatible group and includes a carbon atom covalently attached to C¹; R^x includes a carbon atom covalently attached to C²; n is an integer; each occurrence of R³, R⁴, R⁵ and R⁶ is a biocompatible group and is independently hydrogen or an organic moiety; and for each occurrence of the bracketed structure n, at least one of R¹, R², R³, R⁴, R⁵ and R⁶ comprises a carbonyl group suitable for oxime formation.

12. (Original) The conjugate of claim 1, wherein the carrier is a biodegradable biocompatible polyketal wherein at least a subset of the polyketal repeat structural units have the following chemical structure:

wherein each occurrence of R^1 and R^2 is a biocompatible group and includes a carbon atom covalently attached to C^1 ; R^x includes a carbon atom covalently attached to C^2 ; n is an integer; each occurrence of R^3 , R^4 , R^5 and R^6 is a biocompatible group and is independently hydrogen or an organic moiety; and for each occurrence of the bracketed structure n, at least one of R^1 , R^2 , R^3 , R^4 , R^5 and R^6 comprises a carbonyl group suitable for oxime formation.

- 13. (Original) The conjugate of claim 1, wherein one or more occurrences of M comprises a biologically active modifier.
- 14. (Currently Amended) The conjugate of elaim 8 claim 13, wherein one or more occurrence of M is selected from the group consisting of proteins, antibodies, antibody fragments, peptides, antineoplastic drugs, hormones, cytokines, enzymes, enzyme substrates, receptor ligands, lipids, nucleotides, nucleosides, metal complexes, cations, anions, amines,

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heterocycles, heterocyclic amines, aromatic groups, aliphatic groups, intercalators, antibiotics, antigens, immunomodulators, and antiviral compounds

15. (Original) The conjugate of claim 1, wherein one or more occurrence of M comprises a

detectable label.

16. (Currently Amended) The conjugate of claim 10 claim 15, wherein one or more

occurrence of M comprises atoms or groups of atoms comprising radioactive, paramagnetic,

superparamagnetic, fluorescent, or light absorbing structural domains.

17. (Currently Amended) The conjugate of claim 1, wherein one or more occurrence of M

comprises a dignostic diagnostic label.

18. (Currently Amended) The conjugate of claim 12 claim 17, wherein one or more

occurrence of M comprises radiopharmaceutical or radioactive isotopes for gamma scintigraphy

and PET, contrast agent for Magnetic Resonance Imaging (MRI), contrast agent for computed

tomography, contrast agent for X-ray imaging method, agent for ultrasound diagnostic method,

agent for neutron activation, moiety which can reflect, scatter or affect X-rays, ultrasounds,

radiowaves, microwaves and/or fluorophores.

19. (Original) The conjugate of claim 1, wherein the conjugate is water-soluble.

20. (Original) The conjugate of claim 1, wherein the conjugate comprises a biologically

active modifier and a detectable label.

21. (Original) The conjugate of claim 1, wherein the carrier is a linear macromolecule, a

branched macromolecule, a globular macromolecule, a graft copolymer, a comb copolymer, a

nanoparticle or a lipid-based carrier.

22. (Currently Amended) The conjugate of claim 16 claim 21, wherein the lipid-based

carrier is a liposome.

- 23. (Original) A compound having the structure $R^{N1}R^{N2}N$ -O- L^1 ; wherein R^{N1} and R^{N2} are independently hydrogen, an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl or heteroaryl moiety, or a nitrogen protecting group, or R^{N1} and R^{N2} , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic or heteroaryl moiety; and L^1 is an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl or heteroaryl moiety comprising a functional group adapted for covalent binding to a modifier.
- 24. (Currently Amended) The compound of elaim 24 claim 23, wherein L¹ is a moiety having the structure –(CR^{L1}R^{L2})_p-Q-, wherein p is an integer from 0-6, R^{L1} and R^{L2} are independently hydrogen, an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl or heteroaryl moiety or WR^{W1} wherein W is O, S, NH, CO, SO₂, COO, CONH, and R^{W1} is hydrogen, an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl, heteroaryl, alkylaryl or alkylheteroaryl moiety, and Q is a moiety comprising a functional group adapted for covalent binding to a modifier.
- 25. (Currently Amended) The compound of claim 25 claim 24, wherein L^1 is- $(CH_2)_p$ wherein p is an integer from 0-5, and Q is a succinimidal ester moiety having the structure:

26. (Currently Amended) The compound of elaim 25 claim 23, wherein L^1 is– $(CH_2)_{p_1}$ - $CH(OH)CH_2NH$ - wherein p_1 is an integer from 1-5, and Q is a maleimidyl moiety having the structure:

wherein p_2 is is an integer from 1-5.

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27. (Currently Amended) The compound of elaim 24 claim 23, wherein R^{N1}R^{N2}N- is a moiety having the structure:

28. (Original) A compound having the structure:

$$R^{N1} \underset{R^{N2}}{\nearrow} O \underset{L^{M1}}{\searrow} M$$

wherein M is a modifier; L^{M1} is a substituted or unsubstituted, cyclic or acyclic, linear or branched C_{0-12} alkylidene or C_{0-12} alkenylidene moiety wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl; and R^{N1} and R^{N2} are independently hydrogen, an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl or heteroaryl moiety, or a nitrogen protecting group, or R^{N1} and R^{N2}, taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic or heteroaryl moiety.

29. (Currently Amended) The compound of elaim 29 claim 28, wherein L^{M1} comprises an NHS ester crosslinker and the compound has the structure:

$$\mathbb{R}^{N_1}$$
 \mathbb{N} \mathbb

wherein p is 0-5.

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30. (Currently Amended) The compound of elaim 29 claim 28, wherein L^4 L^{M1} comprises a maleimide crosslinker and the compound has the structure:

$$\mathbb{R}^{\mathbb{N}^2}$$
 \mathbb{N} \mathbb{N}

wherein p_1 and p_2 are independently integers from 1-5.

31. (Currently Amended) The compound of claim 29, 30 or 31 claim 28, 29 or 30, wherein $R^{N1}R^{N2}N$ - is a moiety having the structure:

32. (Original) A method for preparing a conjugate comprising a carrier substituted with one or more occurrences of a moiety having the structure:

wherein each occurrence of M is independently a modifier; and each occurrence of L^M is independently an oxime-containing linker; said method comprising steps of: providing a carrier; providing one or more modifiers;

providing one or more compounds having the structure: $R^{N1}R^{N2}N$ -O- L^{1} ; wherein R^{N1} and R^{N2} are independently hydrogen, an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl or heteroaryl moiety, or a nitrogen protecting group, or R^{N1} and R^{N2} , taken together, form a substituted or unsubstituted alicyclic, aryl or heteroaryl moiety; and each occurrence of L^{1} is independently an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl or heteroaryl moiety comprising a functional group adapted for covalent binding to the modifier; and

reacting the one or more compounds of structure R^{N1}R^{N2}N-O-L¹ with the carrier and the one or more modifiers under suitable conditions so that at least one –O-NR^{N1}R^{N2} moiety is covalently attached to the carrier via an oxime linkage, thereby generating the conjugate.

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Client Reference: MGH 2170 US

33. (Original) A method for preparing a conjugate comprising a carrier substituted with one or more occurrences of a moiety having the structure:

wherein each occurrence of M is independently a modifier; and each occurrence of L^M is independently an oxime-containing linker; said method comprising steps of:

providing a carrier;

providing one or more compounds having the structure:

$$R^{N1}$$
 O L^{M1} M

wherein L^{M1} is a substituted or unsubstituted, cyclic or acyclic, linear or branched C₀. 1₂alkylidene or C₀₋₁₂alkenylidene moiety wherein up to two non-adjacent methylene units are independently optionally replaced by CO, CO₂, COCO, CONR^{Z1}, OCONR^{Z1}, NR^{Z1}NR^{Z2}, NR^{Z1}NR^{Z2}CO, NR^{Z1}CO, NR^{Z1}CO₂, NR^{Z1}CONR^{Z2}, SO, SO₂, NR^{Z1}SO₂, SO₂NR^{Z1}, NR^{Z1}SO₂NR^{Z2}, O, S, or NR^{Z1}; wherein each occurrence of R^{Z1} and R^{Z2} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or acyl; and R^{N1} and R^{N2} are independently hydrogen, an aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl or heteroaryl moiety, or a nitrogen protecting group, or R^{N1} and R^{N2}, taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic or heteroaryl moiety; and

reacting the carrier with the one or more compounds of structure:

$$\begin{array}{c|c}
R^{N1} & O & M
\end{array}$$

under suitable conditions so that at least one -O-NR^{N1}R^{N2} moiety is covalently attached to the carrier via an oxime linkage, thereby generating the conjugate.

34. (Original) The method of claim 32 or 33, wherein R^{N1} and R^{N2} are each hydrogen.

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- 35. (Original) The method of claim 32, wherein in the one or more compounds of structure $R^{N1}R^{N2}N$ -O-L¹; at least one of R^{N1} and R^{N2} is a nitrogen protecting group; and the method further comprises the step of hydrolyzing the one or more compounds having the structure $R^{N1}R^{N2}N$ -O-L¹ to form one or more compounds having the structure H_2N -O-L¹ prior to reacting with the carrier.
- 36. (Original) The method of claim 35, wherein in the one or more compounds of structure $R^{N1}R^{N2}N$ -O-L¹, $R^{N1}R^{N2}N$ has the structure $CH_3CH_2OC(CH_3)$ =N-; and the one or more compounds have the following structure:

37. (Original) The method of claim 33, wherein in the one or more compounds of structure

$$\begin{array}{c|c}
R^{N1} & O & M \\
\downarrow & & M
\end{array}$$

at least one of R^{N1} and R^{N2} is a nitrogen protecting group; and the method further comprises the step of hydrolyzing the one or more compounds having the structure:

$$\begin{array}{c|c}
R^{N1} & O & M
\end{array}$$

to form one or more compounds having the structure:

prior to reacting with the carrier.

38. (Original) The method of claim 37, wherein in the one or more compounds of structure:

R^{N1}R^{N2}N- has the structure CH₃CH₂OC(CH₃)=N-; and the one or more compounds have the

following structure:

$$O$$
 N
 O
 L^{M1}
 M

39. (Original) The method of claim 32 or 33, wherein the carrier is a biodegradable biocompatible polyacetal wherein at least a subset of the polyacetal repeat structural units have the following chemical structure:

wherein for each occurrence of the n bracketed structure, one of R¹ and R² is hydrogen, and the other is a biocompatible group and includes a carbon atom covalently attached to C¹; R^x includes a carbon atom covalently attached to C²; n is an integer; each occurrence of R³, R⁴, R⁵ and R⁶ is a biocompatible group and is independently hydrogen or an organic moiety; and for each occurrence of the bracketed structure n, at least one of R¹, R², R³, R⁴, R⁵ and R⁶ comprises an aldehyde moiety.

40. (Original) The method of claim 32 or 33, wherein the carrier is a biodegradable biocompatible polyketal wherein at least a subset of the polyketal repeat structural units have the following chemical structure:

$$- \underbrace{ \begin{bmatrix} R^1 & R^3 & R^5 \\ C^1 & C_2 & R^x \end{bmatrix}_n}_{R^2} \qquad \underbrace{ \begin{bmatrix} R^1 & C_1 & C_2 & R^x \end{bmatrix}_n}_{Or} \qquad \underbrace{ \begin{bmatrix} R^1 & C_1 & C_2 & R^x \end{bmatrix}_n}_{Or}$$

wherein each occurrence of R^1 and R^2 is a biocompatible group and includes a carbon atom covalently attached to C^1 ; R^x includes a carbon atom covalently attached to C^2 ; n is an integer; each occurrence of R^3 , R^4 , R^5 and R^6 is a biocompatible group and is independently hydrogen or an organic moiety; and for each occurrence of the bracketed structure n, at least one of R^1 , R^2 , R^3 , R^4 , R^5 and R^6 comprises an aldehyde moiety.

- 41. (Original) A composition comprising the conjugate of claim 1 and a pharmaceutically suitable carrier or diluent.
- 42. (Original) A composition comprising a conjugate of claim 1 associated with an effective amount of a therapeutic agent; wherein the therapeutic agent is incorporated into an released from said conjugate matrix by degradation of the conjugate matrix or diffusion of the agent out of the matrix over a period of time.
- 43. (Original) The composition of claim 42 wherein said conjugate is further associated with a diagnostic agent.
- 44. (Currently Amended) A method of administering to a patient in need of treatment, comprising administering to the subject an effective amount of a suitable therapeutic agent; wherein said therapeutic agent is associated with and released from a conjugate of elaims 1 claim 1 by degradation of the conjugate matrix or diffusion of the agent out of the matrix over a period of time.
- 45. (Original) The method of claim 44 wherein said therapeutic agent is locally delivered by implantation of said conjugate matrix incorporating the therapeutic agent.
- 46. (Original) The method of claim 44 wherein said therapeutic agent is selected from the group consisting of: vitamins, anti-AIDS substances, anti-cancer substances, antibiotics, immunosuppressants, anti-viral substances, enzyme inhibitors, neurotoxins, opioids, hypnotics, anti-histamines, lubricants, tranquilizers, anti-convulsants, muscle relaxants and anti-Parkinson substances, anti-spasmodics and muscle contractants including channel blockers, miotics and anti-cholinergics, anti-glaucoma compounds, anti-parasite and/or anti-protozoal compounds, modulators of cell-extracellular matrix interactions including cell growth inhibitors and anti-adhesion molecules, vasodilating agents, inhibitors of DNA, RNA or protein synthesis, anti-hypertensives, analgesics, anti-pyretics, steroidal and non-steroidal anti-inflammatory agents, anti-angiogenic factors, anti-secretory factors, anticoagulants and/or antithrombotic

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agents, local anesthetics, ophthalmics, prostaglandins, anti-depressants, anti-psychotic substances, anti-emetics, imaging agents.

- 47. **(Original)** The method of claim 44 further comprising administering with the therapeutic agent additional biologically active compounds selected from the group consisting of vitamins, anti-AIDS substances, anti-cancer substances, antibiotics, immunosuppressants, anti-viral substances, enzyme inhibitors, neurotoxins, opioids, hypnotics, anti-histamines, lubricants, tranquilizers, anti-convulsants, muscle relaxants and anti-Parkinson substances, anti-spasmodics and muscle contractants including channel blockers, miotics and anti-cholinergics, anti-glaucoma compounds, anti-parasite and/or anti-protozoal compounds, modulators of cell-extracellular matrix interactions including cell growth inhibitors and anti-adhesion molecules, vasodilating agents, inhibitors of DNA, RNA or protein synthesis, anti-hypertensives, analgesics, anti-pyretics, steroidal and non-steroidal anti-inflammatory agents, anti-angiogenic factors, anti-secretory factors, anticoagulants and/or antithrombotic agents, local anesthetics, ophthalmics, prostaglandins, anti-depressants, anti-psychotic substances, anti-emetics, imaging agents, and combination thereof.
- 48. (Original) The method of claim 44 wherein said conjugate further comprises or is associated with a diagnostic label.
- 49. **(Original)** The method of claim 48 wherein said diagnostic label is selected from the group consisting of: radiopharmaceutical or radioactive isotopes for gamma scintigraphy and PET, contrast agent for Magnetic Resonance Imaging (MRI), contrast agent for computed tomography, contrast agent for X-ray imaging method, agent for ultrasound diagnostic method, agent for neutron activation, moiety which can reflect, scatter or affect X-rays, ultrasounds, radiowaves and microwaves and fluorophores.
- 50. (Original) The method of claim 48 wherein said conjugate is further monitored in vivo.

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51. (Original) A method of administering a conjugate of claim 1 to an animal, comprising

preparing an aqueous formulation of said conjugate and parenterally injecting said formulation in

the animal.

52. (Original) The method of claim 51, wherein said conjugate comprises a biologically

active modifier.

53. (Original) The method of claim 51, wherein said conjugate comprises a detectable

modifier.

54. (Original) A method of administering a conjugate of claim 1 to an animal, comprising

preparating preparing an implant comprising said conjugate, and implanting said implant into the

animal.

55. (Original) The method of claim 54, wherein said implant is a biodegradable gel matrix.

56. (Original) A method for treating of an animal in need thereof, comprising administering

a conjugate as in claim 51 or 54, wherein said conjugate is associated with a biologically active

component.

57. (Original) A method for treating of an animal in need thereof, comprising administering

a conjugate as in claim 51 or 54, wherein said conjugate comprises a biologically active

modifier.

58. (Original) The method of claim 57, wherein the biologically active component is a gene

vector.

59. (Original) A method for eliciting an immune response in an animal, comprising

administering a conjugate as in claim 51 or 54, wherein said conjugate comprises an antigen

modifier.

- 60. (Original) A method of diagnosing a disease in an animal, comprising steps of:
 administering a conjugate as in claim 51 or 54, wherein said conjugate comprises a
 detectable modifier; and
 detecting the detectable modifier.
- 61. (Original) The method of claim 60, wherein the step of detecting the detectable modifier is performed non-invasively.
- 62. (Original) The method of claim 61, wherein the step of detecting the detectable modifier is performed using suitable imaging equipment

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